Combinatorial Search for Artificial Receptors of Neurotransmitters based on Lipid Nanoemulsions

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Résumé

Neurotransmitters (NTs) are chemical messengers responsible for the communication between neurons throughout the human body. NTs are essential to the proper function of the nervous system as well as the communication of organs with the nervous system. Abnormal levels of NTs can therefore be tied to a variety of physiological and neurological disorders, so that the detection of such imbalances is of high interest. However, the recognition of small molecules in complex mixtures remains a challenging endeavor. In nature, the recognition of NTs is performed by protein receptors containing highly structured and functionalized binding sites selective to their target. Lipid nanoemulsions (LNEs) have shown to be promising artificial receptors for dopamine when loaded with a boronic acid as recognition ligand (RL) selective to catechol moieties. Following this line of research, we intend to mimic natural biding sites by incorporating hydrophobic analogues of common amino acid side chains as RLs, where the capture of the hydrophilic analytes in the lipid nanoreactors is performed through supramolecular interactions with the RLs such as hydrogen bonding, electrostatic interactions or π-π stacking. Inspired by biological protein receptors, we developed a library of lipophilic decarboxylated amino-acid derivatives (AAs). A combinatorial strategy and high throughput spectroscopy methods, based on the emission shift of an aldehyde dye sensitive to primary amines, were used to find AA mixtures with an emergent affinity and selectivity towards the following NTs: dopamine, histamine, noradrenaline and serotonin. Using this approach, we first discovered that LNEs loaded with our glutamic acid analogue (EC16) showed higher capture of NTs than other RLs. Secondly, mixtures of EC16 with the glutamine analogue (GC16) and EC16 with the methionine analogue (MC16) displayed a higher capture of NTs than EC16 alone and an emergent selectivity towards dopamine. To further improve the sensitivity of our probe and to emulate the 3D structure of biological protein receptors, we intend to add hydrogen-binding groups to the RLs. Thus, causing them to pre-organize in the LNEs, which adds structural recognition to the already demonstrated functional recognition of our probe.

Mots-Clés: nanoemulsions, neurotransmitters, artificial receptors, molecular recognition, supramolecular chemistry, combinatorial chemistry

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